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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Noelle Mistretta

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EXAMINER

OLSON, ERIC

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/758,142	Applicant(s) MISTRETTE ET AL.	
	Examiner ERIC S. OLSON	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,8 and 10-31 is/are pending in the application.
- 4a) Of the above claim(s) 11-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 8, 10, 30, and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 1, 2009 has been entered.

Detailed Action

This office action is a response to applicant's communication submitted June 1, 2009 wherein claims 1, 10, and 31 are amended and claims 2-7 and 9 are cancelled. This application claims benefit of provisional application 60/442154, filed January 22, 2003, and claims priority to foreign application FR0300488, filed January 17, 2003.

Claims 1, 8, and 10-31 are pending in this application.

Claims 11-29 are withdrawn from consideration as being directed to non-elected subject matter.

Claims 1, 8, 10, 30, and 31 as amended are examined on the merits herein.

Applicant's amendment, submitted June 1, 2009, with respect to the rejection of instant claims 1, 2, 5-7, 9, 10, 30, and 31 under 35 USC 102(b) for being anticipated by Moreau et al., has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to encompass only reduced capsular

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polysaccharide having no ketone groups (the signal at 11.5-12.5 ppm in the NMR spectra recited in claim 1) which would not result from the methods disclosed by Moreau et al. alone. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8, 10, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moreau (US patent 6596861, of record in previous office action,

previously published on September 21, 2000 as WO00/55210) in view of Jansson et al. (of record in previous office action)

Moreau teaches a method for the reductive amination of polysaccharide useful in a process for conjugating polysaccharides to polypeptides (co1.1, lines 1-4). Moreau discloses the aminated capsular polysaccharide of *Streptococcus pneumoniae* of serotype 5 (col. 6, lines 60-61). Regarding claims 10, 30 and 31, the prior art discloses that the aminated polysaccharide can be conjugated to a polypeptide per se (co1.8, lines 60-61). Moreau also discloses the reductive amination of acidic (negatively charged) polysaccharide (co1.10, Example 1). Moreau discloses the pharmaceutical composition of said compounds and their conjugates thereof (col.10, lines 24-29). Moreau et al. does not disclose a polysaccharide conjugate that lacks the ^{13}C peak between 11.5 and 12.5 ppm described in instant claim 1, or a structure according to instant claim 8 wherein A is CHOH.

Regarding the structural and NMR characteristics of the polysaccharide produced by Moreau et al., the specification as originally filed discloses an inventive example (example 1, p. 34) that is typical of the claimed invention, wherein a pH 6.0 reaction buffer containing the type 5 polysaccharide , an amine, and sodium cyanoborohydride, is incubated at 50°C for 2 hours. The specification (p. 17 line 24 – p. 18 line 7) further discloses that the formation of undesirable byproducts is a function of time, with compound X being observed for incubation times of greater than 4 hours. This method is equivalent to a method disclosed as the "first method" in the specification and disclosed on pp. 12-13 and 15-16 as producing a product containing

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at least 95% of A = C=O groups and having a ^{13}C resonance between 11.5 and 12.5 ppm.

Furthermore the "second method" described in the specification involving reduction of the carbonyls in the Sug residue (see pp. 14-16) is disclosed to result in a product in which the C=O group is completely reduced to CHOH and the 11.5-12.5 NMR peak is consequently absent. Therefore the NMR limitations disclosed in claim 1 indicate that the structure is the structure recited in claim 8 as amended.

Regarding the 13-14 ppm peak, this peak is disclosed on p. 13 lines 25-26 to be indicative of the unidentified "compound X". As discussed in the previous office actions, compound X is disclosed, in Applicant's specification and previous arguments made in the prosecution of this application, to be introduced into the product by long reaction times. Therefore no product prepared by the method of Moreau et al. (which uses reaction times that are at most equivalent to those disclosed in the instant specification) will exhibit this NMR signal.

Jansson teaches the repeating-unit structure of *Streptococcus pneumoniae* type 5 capsular polysaccharide composed of glucose, N-acetylated fucosamine, N-acetylated pneumosamine (2-acetamido-2,6-deoxytalose), glucuronic acid and Sug (2-acetamido- 2,6-deoxyhexose-4-ulose) (page 101, abstract). Jansson discloses the ^1H and ^{13}C -NMR spectra characterizing the polysaccharide structure (page 103, fig. 1 and page 107). Jansson also discloses borohydride reduction of *Streptococcus pneumoniae* type 5 capsular polysaccharide to obtain the product having similar immunological activity, which can also be used as a vaccine, and suggests that this product would

have a superior stability and reduced base-lability. (page 107, last para. to page 108, lines 1-3; page 108, last paragraph)

It would have been obvious to person having ordinary skill in the art at the time the invention was made to produce conjugates of *S. pneumonidae* type 5 capsular protein with a carrier polypeptide by reductive amination according to Moreau et al., with prior borohydride treatment, thus producing conjugates of the A = CHOH structure II", and to incorporate this conjugate into a pharmaceutical composition, such as a vaccine. One of ordinary skill in the art would have been motivated to produce these compounds and compositions because Moreau teaches a method for the reductive amination of polysaccharide useful in a process for conjugating polysaccharides to polypeptides; and Jansson teaches reduced *Streptococcus pneumoniae* type 5 capsular polysaccharide that has reduced degradation and browning on storage. One of ordinary skill in the art would reasonably have expected success because the chemical transformations described by Moreau and Jansson are well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted June 1, 2009, with respect to the above ground of rejection have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the prior art provides no reason to reduce the ketone functions of the polysaccharide prior to reductive amination. However, Jansson et al. clearly discloses that reducing these functionalities would be expected to improve the stability of the resulting conjugate. Also note that,

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with regard to the sequence of the reduction and reductive amination steps, performing the borohydride reduction on the conjugated product after the reductive amination would produce the same ketone-reduced product as does the method in the specification without necessitating an additional fragmentation step. Because the claims are drawn to a product and not to a method of making said product, the exact order of steps used to make a particular product does not matter as to whether the product of the method renders the claims obvious.

Therefore the rejection is deemed proper and maintained.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
9/4/2009